

REMARKS**I. Status of the Claims**

Claim 1 is amended.

Claim 1 is pending.

Claims 2-27 were previously withdrawn in response to a restriction requirement.

II. A *Prima Facie* Case Obviousness Over Taylor-Papadimitriou *et al.*, Is Not Established.

On page 4 of the Office Action ("Action"), the examiner rejected claim 1 under § 103(a) as being unpatentable over Taylor-Papadimitriou *et al.* The examiner believes that Taylor-Papadimitriou *et al.*, disclose a cancer associated antigen MUC1. The examiner refers to Table 1 and left column of page 228 in Taylor-Papadimitriou *et al.* However, neither this table nor the text teaches a method of identifying cancer-associated peptide antigens comprising mapping hydrophilic region and identifying sites that are de-glycosylated in cancer cells, and preparing labeled synthetic peptides.

To properly combine two references to reach a conclusion of obviousness, there must be some teaching, suggestion or inference in either or both of the references, or knowledge generally available to one skilled in the art, which would have led one to combine the relevant teachings of the two references. *Ashland Oil, Inc. v. Delta Resins and Refractories, Inc. et al.* (CAFC 1985) 776 F. 2d 281, 227 USPQ 657; *Ex parte Levengood, supra*. Both the suggestion to make the claimed composition or device or carry out the claimed process and the reasonable expectation of success must be founded in the prior art, not in applicant's disclosure. *In re Vaeck* (CAFC 1991) 947 F. 2d 488, 20 PQ. 2d 1438. **Citing references which merely indicate that isolated elements and/or features recited in the claims are known is not a sufficient basis for concluding that the combination of claimed elements would have been obvious, *Ex parte Hiyamizu* (BPAI 1988) 10**

PQ. 2d 1393 (*emphasis provided*), absent evidence of a motivating force which would impel persons skilled in the art to do what applicant has done. *Ex parte Levengood* (BPAI 1993) 28 PQ. 2d 1300. The references, viewed by themselves and not in retrospect, must suggest doing what applicant has done. *In re Shaffer* (CCPA 1956) 229 F. 2d 476, 108 USPQ 326; *In re Skoll* (CCPA 1975) 523 F. 2d 1392, 187 USPQ 481. The examiner has not demonstrated teachings to combine Taylor-Papadimitriou *et al.* with teaching in the art.

Taylor-Papadimitriou *et al.*, describe the changes in glycosylation and expression of mucins with particular emphasis on polymorphic epithelial mucin (PEM), the product of the MUC1 gene in tumors and normal tissues. Table 1 in Taylor-Papadimitriou *et al.*, to which the examiner refers, shows sequences of the tandem-repeat units of human mucins, and the left column of page 228 describes enzymes and pathways involved in the synthesis of the relevant gangliosides, detection of short sugar side chains such as Ser/Thr-GalNac on cancer cells, and monoclonal antibodies that react with mucins. Contrary to the examiner's view, Table 1 and page 228 left column of Taylor-Papadimitriou *et al.*, do not disclose a transmembrane protein with an extracellular domain that is hydrophilic, nor is any suggestion of the elements of the method of claim 1 of the present invention. For example, there is no teaching of a receptor or a receptor-like molecule as in claim 1, step (a) and synthetic peptides as in step (e).

The examiner admits:

While Taylor-Papadimitriou *et al.* do not explicitly disclose the details of step (a)-(b) and (e)-(g)

Action, page 4

but argues that the steps "are well-recognized skills in the art" referring, *e.g.* to Hopp and Woods.

The legal standard for a *prima facie* case of obviousness is **not** to show that all individual elements of a claim are known to those of skill in the art (which in any case the examiner has **not**

proved) but to show a teaching or suggestion to combine the elements. The examiner fails to make the showing, no evidence is given, therefore a *prima facie* case of obviousness is not established.

On page 4 of the Action, the examiner states that a person of ordinary skill in the art, with the knowledge of MUC1, would have been motivated to search other proteins/peptides with an altered pattern of glycosylation in cancer cells. It would be a major jump in logic from the statement in Taylor- Papadimitriou *et al.* that changes in glycosylation makes it "now possible to make a more directed approach to exploiting them in the diagnosis and treatment of cancer," to steps a-g of claim 1.

To establish *prima facie* obviousness of a claimed invention, **all the claim limitations must be taught or suggested by the prior art.** In *re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970) (*emphasis added*).

The sequence of steps (a)-(g), which is to practice the claimed invention is neither taught nor suggested in Taylor-Papadimitriou *et al* or Hopp and Woods, or their combination.

Moreover, on page 4 of the Action, the examiner, quoting from Taylor-Papadimitriou states that Taylor-Papadimitriou *et al.*, would motivate a person of ordinary skill in the art to exploit the knowledge of the role of glycosylation in cancer diagnosis and treatment.

A statement that modifications of the prior art to meet the claimed invention would have been " 'well within the ordinary skill of the art at the time the claimed invention was made' " because the references relied upon teach that all aspects of the claimed invention were individually known in the art **is not sufficient to establish a *prima facie* case of obviousness** without some objective reason to combine the teachings of the references. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). See also *In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1318 (Fed. Cir. 2000) (*emphasis added*).

In the present action, the examiner merely states his opinion and does not offer evidentiary support how knowledge of the role of glycosylation will motivate a person of ordinary skill in the art to obtain hydrophilic sequence of the extracellular domain of a receptor or receptor-like molecule,

performing rolling sum analysis, locating amino acids that are susceptible to modification in the absence of steric hindrance by glycoside chains, and synthesizing those peptides and testing by an *in vitro* assay that the peptides are cancer-specific or cancer associated as disclosed in claim 1.

On page 230, right column, Taylor-Papadimitriou *et al.*, state:

It should be noted, however, that the same mucin **may be glycosylated differently by different normal tissues**. [T]his degree of complexity means that analysis of mucin expression with antibodies can be difficult to interpret. (*emphasis added*).

Therefore, a mere knowledge of the role of glycosylation is not enough to motivate a person of ordinary skill in the art to practice the claimed invention, which is to differentiate normal cells from cancer cells.

On page 4 of the Action, the examiner, while acknowledging that Taylor-Papadimitriou *et al.*, do not disclose all the elements of claim 1, states that Hopp and Woods teach a rolling sum analysis of six or more consecutive residues to predict antigenic region of a peptide sequence and therefore the claimed method would have been obvious to one of ordinary skill in the art with a reasonable expectation of success at the time of the invention.

Citing references which merely indicate that isolated elements and/or features recited in the claims are known is not a sufficient basis for concluding that the combination of claimed elements would have been obvious *Ex parte Hiyamizu* (BPAI 1988) 10 PQ. 2d 1393.

Hopp and Woods merely disclose a method to predict protein antigenic determinants from amino acid sequences by assigning hydrophilicity values to adjacent amino acid residues. Rolling sum analysis to map hydrophilic regions is just one step in the claimed method. Hopp and Woods do not teach or suggest any other steps in claim 1. For example, locating amino acids that are susceptible to modification in the absence of steric hindrance is neither taught nor suggested by Hopp and Woods.

The references, viewed by themselves and not in retrospect, must suggest doing what applicant has done. *In re Shaffer* (CCPA 1956)

229 F. 2d 476, 108 USPQ 326; *In re Skoll* (CCPA 1975) 523 F. 2d 1392, 187 USPQ 481.

Therefore, even if Taylor-Papadimitriou *et al.*, and Hopp and Woods were combined, a person of ordinary skill in the art would not have come up with the claimed invention.

Applicant requests withdrawal of the 103 (a) rejection.

III. Other issues

Claim 1 is amended to include examiner's suggestion for proper antecedents.

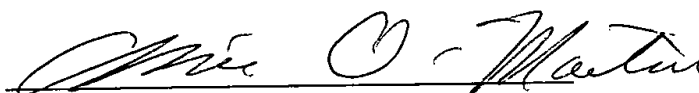
The list of references on pages 35-37 of the specification was not meant to substitute for an Information Disclosure Statement. An IDS was filed on April 10, 2001.

Applicants request allowance of the pending claim.

No other fees are believed due at this time, however, please charge any deficiencies or credit any overpayments to deposit account number 12-0913 with reference to our attorney docket number (21417/91482).

Respectfully submitted,

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